Writing Your Research Plan

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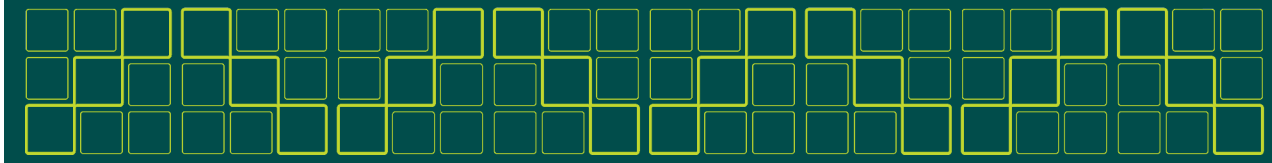

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The Psychology of Grant Review

- Reviewers are:
  - Over-committed, over-worked and tired
  - Inherently skeptical and critical
  - Often only peripherally interested in your work
- Make their job easier with:
  - Well-organized, clearly written prose
  - Lots of section headings and breaks in the writing
  - Repeat important points at several places in the application
  - Well designed flow diagrams, charts, figures
- And avoid irritating them by:
  - Exceeding page limits, using small fonts and narrow margins
  - Putting information in the wrong section
  - Omitting or mislabeling references/figures
  - Submitting an application that is sloppy or full of typographical errors

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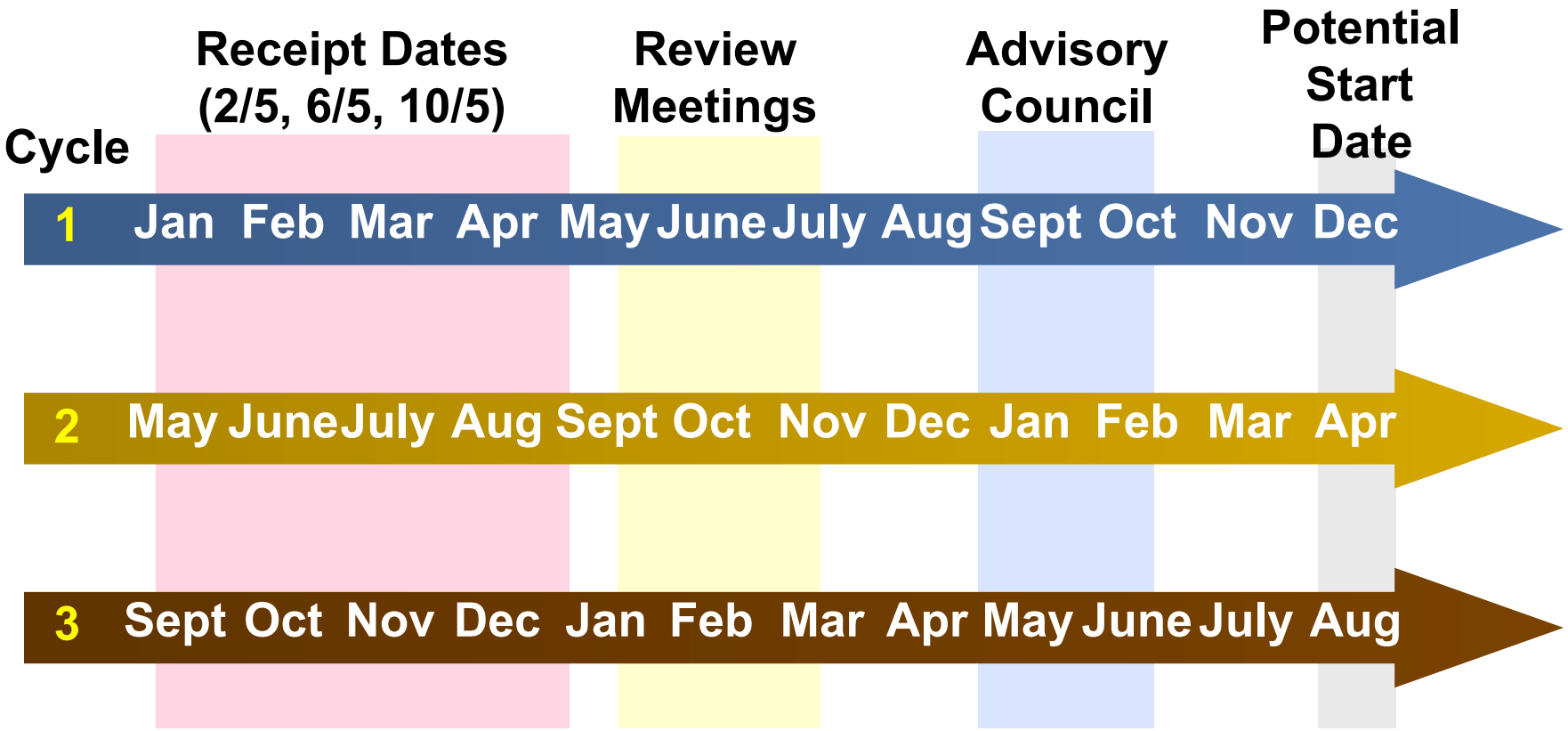
Three NIH Grant Cycles Per Year



The Organizational Process

"Many of us when confronted by a writing deadline, skip the organizational phase of writing. This is akin to leaving on a trip to unknown parts without a road map, hotel reservations, or plans of any sort."

Successful Scientific Writing by Matthews and Mathews (Cambridge University Press)

Decisions to make early

- Identify a funding Institute
  - Where do you want to target your application?
  - Who are the appropriate Program Officers?
  - Note that each Institute has a different pay line
- Select the appropriate funding mechanism
  - Career Development/Transition Awards
  - Research Project Grants (e.g., R01)
  - Consider if a specific RFA is available in your field
- Identify an appropriate Scientific Review Group
  - Depends on Scientific Area
  - CSR Rosters are available online

Getting Started: Administration Issues

- Download and carefully read all instructions and deadlines
  - Important to get latest materials - especially now
- Register for government internet based application and award systems, particularly the eRA Commons
- Talk with lab/department administrators about budgeting, all required approvals, and routing procedures
  - Begin approvals process well in advance of the deadline
- Contact collaborators and arrange for letters as needed

Getting Started: Science Issues

- Read the literature broadly - not deeply; save important papers for a deeper read later
- Engage your lab, mentors, collageagues, and collaborators in the brainstorming process
- Find outside experts to talk with - but go prepared
- Talk with the relevant NIH Program Officer(s)
- Begin early to define, organize and plan the content

- NOTE: Early means 6 - 9 months before the deadline

More Science Issues

- Look hard at your publications - any that need to be submitted NOW?
  - Insufficient publication record is a common concern during review
- Identify ‘need to have’ preliminary data
- Identify methods you need to learn more about or develop expertise in
  - Ideally will will know, or know someone who knows, all the methods you propose
- Make lists of reagent, cell type, animal, or human subject issues you need to deal with
  - Critical reagents must me in-hand

What makes a research project fundable?

- Clearly addresses an important problem
  - Typically not more than one
- Driven by a focused and testable hypothesis
- Asks questions that prove or disprove a hypothesis rather than search for a problem or simply collect information.
- Lays the foundation for further research in the field, opens up new fields, or impacts the way we view a problem
- All aspects of the project are clearly linked
- You seem like the ‘right person’ to do it
  - Now is not the time to pitch new ideas

Strategies To Keep in Mind

- Find information on formats, page limits, and rules in advance, NOT after writing your first draft
- Understand the review criteria from the outset and keep these in mind as you are writing

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Page Limits

Introduction Except Intro to Resubmission for Ts, K12 and R25	1 page
Specific Aims	1 page
Research Strategy R03, R13/U13, R21, R36, R41, R43, Fs, SC2, SC3	6 pages
Research Strategy R01, single project U01, R10, R15, R18, U18, R21/R33, R24, R33, R34, U34, R42, R44, DP3, G08, G11, G13, UH2, UH3, SC1	12 pages
Candidate Information + Research Strategy Career Development Awards (Ks, except K12)	12 pages
Research Training Program Plan Including NRSA (Ts), K12 and R25	25 pages

Restructured Research Plan

Introduction

Specific Aims

Background and Significance

Preliminary Studies/Progress Report

Research Design and Methods

Research Strategy

Inclusion Enrollment Report

Progress Report Publication List

Human Subjects Sections

protections, women/minorities, enrollment, children

Other Research Plan Sections

animals, select agent, consortium, support, sharing

Appendix

Restructured Research Plan

Previous Application	Current Application
Background and Significance	**Research Strategy** a. Significance b. Innovation c. Approach • Preliminary Studies for New Applications • Progress Report for Renewal/Revision
Preliminary Studies/Progress Report	
Research Design and Methods	

What Reviewers Evaluate for Research Grants

- Overall Impact
- "Core" Criteria
  - Significance
  - Investigators
  - Innovation
  - Approach
  - Environment
- Additional Issues (e.g. Human Subjects Protections)

Overall Impact

- Reflects the reviewer's assessment of the likelihood for the project to exert a sustained, powerful influence on the research field(s) involved
- Based on the five core review criteria
  - and additional review criteria as applicable for the project proposed
- An application does not need to be strong in all categories to be judged likely to have major scientific impact.
  - For example, a project that by its nature is not innovative may be essential to advance a field.

Significance

- Does the project address an important problem or a critical barrier to progress in the field?
- If the aims of the project are achieved, how will scientific knowledge, technical capability, and/or clinical practice be improved?
- How will successful completion of the aims change the concepts, methods, technologies, treatments, services, or preventative interventions that drive this field?

Investigator(s)

- Are the PIs, collaborators, and other researchers well suited to the project?
- If Early Stage Investigators or New Investigators, do they have appropriate experience and training?
- If established, have they demonstrated an ongoing record of accomplishments that have advanced their field (s)?
- If the project is collaborative or multi-PD/PI, do the investigators have complementary and integrated expertise; are their leadership approach, governance and organizational structure appropriate for the project?

Innovation

- Does the application challenge and seek to shift current research or clinical practice paradigms by utilizing novel theoretical concepts, approaches or methodologies, instrumentation, or interventions?
- Are the concepts, approaches or methodologies, instrumentation, or interventions novel to one field of research or novel in a broad sense?
- Is a refinement, improvement, or new application of theoretical concepts, approaches or methodologies, instrumentation, or interventions proposed?

Approach

- Are the overall strategy, methodology, and analyses well-reasoned and appropriate?
- Are potential problems, alternative strategies, and benchmarks for success presented?
- If the project is in the early stages of development, will the strategy establish feasibility and how will particularly risky aspects be managed?
- If the project involves clinical research, are the plans for protection of human subjects, and inclusion of minorities and members of both sexes/genders, and the inclusion of children, justified in terms of the scientific goals and research strategy proposed?

Environment

- Will the scientific environment in which the work will be done contribute to the probability of success?
- Are the institutional support, equipment and other physical resources available to the investigators adequate for the project proposed?
- Will the project benefit from unique features of the scientific environment, subject populations, or collaborative arrangements?

Specific Aims

- Provides an overview of the details - tells what your proposal is about, and how you will get there
  - start with 1 - 2 paragraph general overview
  - then list AIMS, each clearly defined
  - end with a brief statement of what you will learn if successful
- The reader must finish this section convinced that the proposed research is significant and that you have a feasible approach
- The aims should be clearly and concisely stated; many also include sub-aims
- Typically 2 - 4 related aims. Later aims should NOT depend on the success of previous aims

Significance & Innovation

- The place to clearly state the importance and innovative-ness of the proposed research
  - Not over- or under-hyped
  - Disease relevance is one, of several approaches
- Looks both backward and forward and points out controversies and discrepancies that your work will address
- Should be appropriately referenced with an honest and balanced discussion of others' work
- Do not underestimate the value of this section. A proposal with a strong research plan will generate little enthusiasm if the problem is not seen as significant.

Approach

- Includes both preliminary results/progress report AND your proposed studies
- Organize by specific aims
- Useful tool: rationale - approach - possible problems
- Clearly discuss controls, both positive and negative
- Show you have thought through issues of feasibility, sample size, patient recruitment, data analysis, etc.
- Include a discussion of expected outcomes, data interpretation, potential problems, and alternate approaches

Preliminary Data or Progress Report

- Key pieces of data to generate excitement and enthusiasm for the proposed studies
- Demonstrates feasibility that you can do what you say you are going to do
- Shows you are a careful scientist who does controls and does not over-interpret data
- Figures should have clear legends and should be large enough for reviewers to easily read
- Consider whether to include key pieces of published data

Keep in Mind

- Reviewers generally assume that new investigators are incapable of conducting experiments if they have not demonstrated previous competence with the methodology.
- Including a timeframe helps provide a framework for understanding your plan
- Reviewers carefully read sections relating to animal use or human subjects

Strong research plans:

- Explicitly state the rationale for the proposed studies
- Never assume reviewers will intrinsically appreciate or understand what you intend
- Use flow diagrams for overview, and for complex experiments and protocols
- Include well-designed, easy to follow tables and figures
- Address priorities if patients, reagents or resources will be limited
- Include a discussion of how the data will be analyzed and interpreted
- Include realistic discussions of pitfalls and provide alternate approaches

Important Point

- It is your goal to get people excited about your research.
  - Let your enthusiasm for your research be reflected in your proposal.
  - If you are not enthusiastic when writing your proposal, it is unlikely the reviewers will see anything different

Other important considerations

- Biosketch
  - Indicate your qualifications to carry out the proposed work
  - Don't "pad" with lots of "in preparation" manuscripts
- Literature cited/Bibliography
  - Be thorough, but critical, in citing previous work in the field
- Letters of collaboration
  - Should be enthusiastically supportive and definitively state what will be provided
  - You may need to write these for your collaborators

Common criticisms - Avoid getting "dinged"

- Rationale for hypothesis or methods not sound
- Models over-hyped as relevant to the human situation
- Diffuse, unfocused or superficial examination of the field
- Unexciting science - an incremental advance for the field
- Mediocre preliminary data that are over-interpreted
- Lack of experience in required methodologies
- Unrealistic amount of work
- Lack of sufficient experimental detail
- Too many irrelevant experimental details
- Insufficient discussion of potential pitfalls and alternate strategies
- Lack of knowledge of published work
- Hard to read - poorly constructed, dense, or filled with typographical/ grammatical errors

What Reviewers Really Say

- This is the first of three very long aims that could make its own proposal. The subaims just go on and on.
- An important question and an elegant approach; however there is no discussion of how many targets are expected, and most importantly, what criteria will be used to select which targets to pursue.
- The new computational tools are not tested in relevant biological systems.
- This is a horizontal contribution to the field.
- The investigator does not pay sufficient attention to feasibility issues, including the enrollment of research subjects and careful attention to inclusion issues.
- Insufficient information is given to indicate how the CART analysis will be implemented, and no discussion of power analysis is given. These omissions are particularly unfortunate.
- The role of these very senior scientists needs to be defined.

Options After a Negative Initial Peer Review

- Appeal of the initial review to the Institute Council/Board
  - Must demonstrate that the initial review was procedurally or scientifically flawed. Objections to scientific interpretations or emphasis do not succeed
  - Generally not a good choice
  - Discuss with Program Officer first
- Submission of an amended application

Amended Applications

- Can submit one amended application
- Must respond to reviewers' criticisms
  - Do not have to agree or make the suggested changes, but must respond to the comments
  - Do not attack the reviewers' competence, abilities, etc. This will only hurt your cause.
- No guarantees that amended application will score better than previous submission
  - Different reviewers
  - Different panel of applications

Revisions

- Give yourself the time and space to feel sad and angry, but appreciate that your colleagues, students, lab members are watching
- Avoid calling or writing your program officer until you have calmed down
- Then read the reviewer's comments CAREFULLY
- You will need to decide whether or not the reviewers show any enthusiasm for your application.
- Talk with:
  - senior scientists with experience reading critiques
  - your program officer

Revisions (II)

- If you decide to re-apply, respond explicitly to the criticisms, indicating how and where you have revised your application.
- If you disagree with the reviewer on certain points, state your arguments in a logical manner without challenging their intelligence or understanding of the research area.
- Your rebuttal is limited to 1 page; begin with a short summary and then address each reviewer's concerns, one-by-one or by grouping similar concerns.

An example - absolute agreement

Reviewer 1 accurately pointed out that we had not sufficiently discussed the detergents used to prepare cell lysates for pull-down and co-immunoprecipitation assays. We now expanded this discussion in AIM 3 of the revised application.

Reviewer 2 pointed out that we lacked a clear way to address the relevance of these protein interactions in an animal model. There are no universally accepted animal models for CF lung disease, but we now include studies in mouse tissues and/or well-differentiated human primary airway epithelial (WD-PAE) cell cultures to further explore the physiological relevance of the interactions we identify.

An Example - Graciously Disagreeing

We wholeheartedly agree with Reviewer 2 that unfocused research can indeed lead to “a quagmire of interacting proteins”**.** However, we have several strategies in place to ensure that we do not go down such a path. Specifically, …….. As proof of principle, our progress since June 2004 clearly indicates that we can rapidly identify important interactions for further analysis. Therefore we have retained the protein interactions screens described in AIM 3 of the original application. However in response to the reviewer’s concerns, we have significantly narrowed our screen.

Conclusion

- Unfortunately, only some of the deserving applications can be funded
- Maximize your chances for success by
  - Planning ahead
  - Remembering your target audiences
  - Showing the reviewers that you've thought about your project
  - Preparing a reader-friendly application
  - Remaining optimistic, and letting your enthusiasm for your science come through
  - Exploring all potential funding mechanisms - internal, foundation, and government

It's About More Than The Science

- Observation I:
  - Strong writing can not compensate for bad ideas, but weak writing easily ruins good ideas
- Observation II:
  - Writing well is a learned skill
  - There are great resources at NIH

Helpful Web Resources

- New OER podcasts: http://grants.nih.gov/podcasts/All_About_Grants/index.htm
- NIH Home page http://www.nih.gov/
- NIH Grant Application Basics (Includes guides, tips, and tutorials) http://grants.nih.gov/grants/grant_basics.htm
- Information on Study Sections http://cms.csr.nih.gov/
- Science magazine GrantsNet http://sciencecareers.sciencemag.org/funding